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09/830,744	06/18/2001	Rolando Barbucci	1757	3626

7590  
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21530 Beechwood  
Circleville, OH 43135

06/04/2003

EXAMINER

KRISHNAN, GANAPATHY

ART UNIT PAPER NUMBER

1623

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Restart -  
Change of Address  
Not changed RP.

### **DETAILED ACTION**

1. The amendment filed December 27, 2002 has been received, entered and carefully considered. The amendment affects the instant application accordingly:
  - (A) Claims 1-4, 13 and 16 have been canceled.
  - (B) New Claim 17 has been added.
  - (D) Claims 12, 14 and 15 have been amended.
  - (E) Comments regarding Office Action have been provided drawn to
    - (a) 112, 2<sup>nd</sup> paragraph rejection, which has been withdrawn;
    - (b) Objection of claims, which has been withdrawn;
    - (c) 102(b) rejection, which has been maintained for the reasons of record;
    - (d) 102(e) rejection, which has been maintained for the reasons of record; &
    - (e) 103(a) rejection, which has been maintained for the reasons of record.
2. Claims 12, 14, 15 and 17 are pending in the case.
3. The text of those sections of title 35, U. S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 102***

1. Claims 15 and 17 stand rejected under 35 U.S.C. 102(b) as being anticipated by Pouyani et al (US Patent No. 5,616,5680) for the reasons already of record on pages 3 and 4 of the Office Action mailed October 2, 2002.

Applicant's arguments filed December 27, 2002 have been fully considered but they are not persuasive. Applicants argue against the rejection of Claim 17 on the grounds that original Claim 4 has been included in Claim 17. Applicants argue that if the rejection was not applied originally to Claim 4, then the rejection now should not be applicable to Claim 17. This argument is not persuasive since original Claim 4 was improper under the 2<sup>nd</sup> paragraph of 35 U.S.C. 112. The subject matter of Claim 4 has been amended and is now included in Claim 17. It is also noted that the subject matter in original Claim 4 was contained in original Claim 3, which was properly rejected as being anticipated by the Pouyani et al patent. Claim 17 now contains all the information that was set forth in original Claim 3.

Applicants further argue that the –NH-NH-moiety, which is disclosed as part of the hydrazide compound in the Pouyani et al patent is not included in the diamine compound of the instant claims. This argument is not persuasive since Claim 17 broadly defines “A” as a linear C<sub>2</sub>-C<sub>6</sub> alkylene chain that may be substituted by amino groups, which may include a –NH-NH-moiety when the formula R<sub>1</sub>NH-A-HNR<sub>2</sub> is considered along with “A” being substituted by an amino group. In order to overcome this rejection, further clarification in Claim 17 of how the amino group is substituted onto the “A” group is required.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a hyaluronic acid molecule which is cross-linked with another hyaluronic acid molecule) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Accordingly, the rejection of Claims 15 and 17 under 35 U.S.C. 102(b) as being anticipated by the Pouyani et al patent is maintained for the reasons of record.

2. Claims 14, 15 and 17 stand rejected under 35 U.S.C. 102(e) as being anticipated by Prestwich et al (US Patent No. 5,874,417) for the reasons already of record on page 4 of the Office Action mailed October 2, 2002.

Applicant's arguments filed December 27, 2002 have been fully considered but they are not persuasive. Applicants argue against the rejection of Claim 17 on the grounds that original Claim 4 has been included in Claim 17. Applicants argue that if the rejection was not applied originally to Claim 4, then the rejection now should not be applicable to Claim 17. This argument is not persuasive since original Claim 4 was improper under the 2<sup>nd</sup> paragraph of 35 U.S.C. 112. The subject matter of Claim 4 has been amended and is now included in Claim 17. It is also noted that the subject matter in original Claim 4 was contained in original Claim 3, which was properly rejected as being anticipated by the Prestwich et al patent. Claim 17 now contains all the information that was set forth in original Claim 3.

Applicants further argue that the –NH-NH-moiety, which is disclosed as part of the hydrazide compound in the Prestwich et al patent is not included in the diamine compound of the instant claims. This argument is not persuasive since Claim 17 broadly defines “A” as a linear C<sub>2</sub>-C<sub>6</sub> alkylene chain that may be substituted by amino groups, which may include a –NH-NH-moiety when the formula R<sub>1</sub>NH-A-HNR<sub>2</sub> is considered along with “A” being substituted by an amino group. In order to overcome this rejection, further clarification in Claim 17 of how the amino group is substituted onto the “A” group is required.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a hyaluronic acid molecule which is cross-linked with another hyaluronic acid molecule) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Accordingly, the rejection of Claims 14, 15 and 17 under 35 U.S.C. 102(e) as being anticipated by the Prestwich et al patent is maintained for the reasons of record.

### ***Claim Rejections - 35 USC § 103***

3. Claims 12, 14, 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prestwich et al (US Patent No. 5,874,417) in view of Galin et al (US Patent No. 5,944,753) for the reasons already of record on pages 5-7 of the Office Action mailed October 2, 2002.

Applicant's arguments filed December 27, 2002 have been fully considered but they are not persuasive. Applicants argue against the rejection of Claim 17 on the grounds that original Claim 4 has been included in Claim 17. Applicants argue that if the rejection was not applied originally to Claim 4, then the rejection now should not be applicable to Claim 17. This argument is not persuasive since original Claim 4 was improper under the 2<sup>nd</sup> paragraph of 35 U.S.C. 112. The subject matter of Claim 4 has been amended and is now included in Claim 17. It is also noted that the subject matter in original Claim 4 was contained in original Claim 3, which was properly rejected as

being unpatentable over the Prestwich et al patent in view of the Galin et al patent .  
Claim 17 now contains all the information that was set forth in original Claim 3.

Applicants further argue that the –NH–NH–moiety, which is disclosed as part of the hydrazide compound in the Prestwich et al patent is not included in the diamine compound of the instant claims. This argument is not persuasive since Claim 17 broadly defines “A” as a linear C<sub>2</sub>–C<sub>6</sub> alkylene chain that may be substituted by amino groups, which may include a –NH–NH–moiety when the formula R<sub>1</sub>NH–A–HNR<sub>2</sub> is considered along with “A” being substituted by an amino group. In order to overcome this rejection, further clarification in Claim 17 of how the amino group is substituted onto the “A” group is required.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a hyaluronic acid molecule may be cross-linked with another hyaluronic acid molecule) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a person of ordinary skill in this art would combine the teachings of the Prestwich et al patent with the teachings of the Galin et al patent since both patents disclose the attachment of other compound groups to hyaluronic acid.

Accordingly, the rejection of Claims 12, 14, 15 and 17 under 35 U.S.C. 103(a) as being unpatentable over the Prestwich et al patent in view of the Galin et al patent is maintained for the reasons of record.

### ***Summary***

4. All the pending claims are rejected.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

### ***Examiner's Telephone Number, Fax Number, and Other Information***

5. For 24 hour access to patent application information 7 days per week, or for filing applications, please visit our website at [www.uspto.gov](http://www.uspto.gov) and click on the button "Patent Electronic Business Center" for more information.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Everett White whose telephone number is (703) 308-4621. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached on (703) 308-4624. The fax phone number for this Group is (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

E. White

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James O. Wilson  
Supervisory Primary Examiner  
**Technology Center 1600**

## DETAILED ACTION

### *Claim Objections*

1. Claim 4 is objected to because of the following informalities: The formula set forth in Claim 4 is incorrect. The formula should be changed to " $[(CH_2)_n-O-(CH_2)_n]_m$ ". In Claim 14, line 3, the term "irom" should be changed to "iron". In Claim 16, line 4, the term 'seimi' is misspelled.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
3. Claims 3 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, Claim 3 recites the broad recitation "A is a C<sub>2</sub> – C<sub>10</sub> linear or branched alkylene chain", and the claim also recites "preferably a C<sub>2</sub> – C<sub>6</sub> chain" which is the narrower statement of the range/limitation.



In Claim 16, lines 3 and 4, the phrase "in solid or semi-solid form according to Claim 3" lacks clear antecedent basis since Claim 3 does not describe a substance having solid or semi-solid form.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

5. Claims 1-3, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Pouyani et al (US Patent No. 5,616,5680).

The Pouyani et al patent discloses covalently crosslinked derivatives of hyaluronate that is prepared by the attachment of a pendant hydrazido group on the hyaluronic acid backbone, which is within the scope of a diamine compound being attached to hyaluronic acid (see column 4, lines 47-49). See the 8<sup>th</sup> paragraph of column 4 wherein the Pouyani et al patent discloses that the coupling of aliphatic or aromatic diamines with hyaluronic acid using carbodiimides such as 1 ethyl-3-(3-dimethylaminopropyl carbodiimide is well known in the art. These diamines of the Pouyani et al patent anticipates the broadly claimed polyamine and diamine of instant Claims 1 and 2. The Pouyani et al patent also discloses adding dihydrazides to hyaluronate (see column 4, lines 66 and 67) whereby the dihydrazides may be represented by formula (II) (see the formula at column 5, line 6) wherein A may be a hydrocarbyl such as alkyl or aryl, or A is a heterohydrocarbyl which also includes

oxygen and nitrogen atoms in addition to carbon atoms. This dihydrazide of the Pouyani et al patent anticipate the diamine having the formula that is set forth in instant Claim 3 when "A" is a C<sub>2</sub> – C<sub>10</sub> linear or branched alkylene chain, substituted with carboxy and amino groups. See column 8, lines 19 and 20 of the Pouyani et al patent whereby it is indicated that the product thereof may be characterized as viscous or gel-like, which anticipates the gel form in instant Claim 13. The Pouyani et al patent further discloses that a crosslinked hyaluronate derivative may be utilized in pharmaceutical compositions (see column 2, lines 35-38), which can be used to treat osteoarthritis (see column 14, 1<sup>st</sup> paragraph), which anticipates instant Claim 15.

6. Claims 1-3 and 13-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Prestwich et al (US Patent No. 5,874,417).

The Prestwich et al patent discloses crosslinked derivatives of hyaluronate that is prepared by the attachment of a dihydrazide represented by the formula (II) at line 45 of column 7 of the Prestwich et al patent wherein "A" is a hydrocarbyl such as alkyl and aryl or A is a heterohydrocarbyl which also includes oxygen and nitrogen atoms in addition to carbon atoms, which anticipates the broadly claimed diamines of the instant claims and the diamine of the formula set forth in instant Claim 3 when "A" is a C<sub>2</sub> – C<sub>10</sub> linear or branched alkylene chain, substituted with carboxy and amino groups. In column 2, lines 41-44, the Prestwich et al patent discloses the cross-linked hyaluronic acid in the form of a gel which anticipate instant Claim 13. Prestwich et al discloses that the hyaluronic acid thereof may be used as an aid in ophthalmic surgery and also as a potential therapy for osteoarthritis in humans, which anticipates Claims 15 and 16 of the instant application (see column 1, lines 38-42). Also see example 10 at column 22 of the Prestwich et al patent wherein a description of how metal ions effect the resulting properties of hydrazides when hyaluronic acid is formed in their presence. At line 66 and 67 of column 22, under Example 10, Prestwich et al discloses the metal ions as copper and iron, which anticipates instant Claim 14 when copper and iron is selected to form the metal complex of cross-linked hyaluronic acid.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-4 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prestwich et al (US Patent No. 5,874,417) in view of Galin et al (US Patent No. 5,944,753).

Applicants claim cross-linked hyaluronic acids obtainable by reaction of the carboxylic groups of hyaluronic acid and a polyamine.

The Prestwich et al patent discloses crosslinked derivatives of hyaluronate that is prepared by the attachment of a dihydrazide represented by the formula (II) at line 45 of column 7 of the Prestwich et al patent wherein "A" is a hydrocarbyl such as alkyl and

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aryl, or A is a heterohydrocarbyl which also includes oxygen and nitrogen atoms in addition to carbon atoms, which embraces the broadly claimed diamines of the instant claims and the diamine of the formula set forth in instant Claim 3 when "A" is a C<sub>2</sub> – C<sub>10</sub> linear or branched alkylene chain, substituted with carboxy and amino groups. The Prestwich patent further discloses that any of the carbon atoms of the alkyl group may be separated from each other with a configuration that may be selected as  $-O-CH_2-CH_2-O-$  (see column 7, line 65 to column 8, line 3), which embraces the polyoxyalkylene chain of the formula  $[(CH_2)_n-O-(CH_2)_n]_m$  that is set forth in instant Claim 3. In column 2, lines 41-44 the Prestwich et al patent discloses the cross-linked hyaluronic acid in the form of a gel which encompass the subject matter of instant Claim 13. Prestwich et al discloses that the hyaluronic acid thereof may be used as an aid in ophthalmic surgery and also as a potential therapy for osteoarthritis in humans, which embraces Claims 15 and 16 of the instant application (see column 1, lines 38-42). Also see example 10 at column 22 of the Prestwich et al patent wherein a description of how metal ions effect the resulting properties of hydrazides when hyaluronic acid is formed in their presence. At line 66 and 67 of column 22, under Example 10, Prestwich et al discloses the metal ions as copper and iron, which embraces the subject matter of instant Claim 14 when copper and iron is selected to form the metal complex of cross-linked hyaluronic acid. The cross-linked hyaluronic acids of the instant claims differ from the cross-linked hyaluronic acids of the Prestwich et al patent by further indicating that the hydroxy groups of the hyaluronic acid are sulphated or hemisuccinylated. The Galin et al patent shows that sulfated hyaluronic acid is well known in the art (see column 6, line 11). Also see example 2 of the Galin et al patent wherein a process step is disclosed whereby heparin (a sulfated polysaccharide) is coupled with a diamine. This process step of Example 2 of the Galin patent embraces the cross-linkage of the sulphated hyaluronic acid of the instant claims since the Galin et al patent teaches the substitution of heparin with sulfated hyaluronic acid. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the hyaluronic acid used to form a cross-linked hyaluronic acid of the Prestwich et al patent with sulfated hyaluronic acid, in view of the recognition in the art, as evidenced by the Galin

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et al patent, that sulfated polysaccharides such as sulfated hyaluronic acid improves the biocompatibility of implants in the anterior chamber of the eye.

***Summary***

9. All the pending claims are rejected.

***Examiner's Telephone Number, Fax Number, and Other Information***

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